

U.S.S.N. 09/482,682
VON SEGGERN *et al.*
PRELIMINARY AMENDMENT

group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3.

Sub. F1
E3
2. (Amended) An isolated nucleic acid molecule, comprising: a sequence of nucleotides encoding an adenovirus tripartite leader (TPL) that comprises (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon, wherein the sequence of nucleotides encoding a TPL is operatively linked to an intron containing an RNA processing signal.

4. (Twice Amended) The isolated nucleic acid molecule of claim 2, wherein said intron is native adenovirus intron 1.

5. (Amended) An isolated nucleic acid molecule, comprising a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein said TPL nucleotide sequence is set forth in SEQ ID NO: 32.

E4
6. (Twice Amended) An isolated nucleic acid molecule, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial exon 1, complete TPL exon 2 and complete TPL exon 3 and further comprising a promoter and a sequence of nucleotides that encodes an adenoviral structural protein, operatively linked to said promoter and said TPL-encoding sequence of nucleotides.

E5
9. (Amended) The isolated nucleic acid molecule of claim 7, wherein said molecule is contained in a plasmid selected from the group consisting of plasmids pDV60, pDV67, pDV69, pDV80 and pDV90.

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E3 10. (Amended) The isolated nucleic acid molecule of claim 9, wherein said molecule has a nucleotide sequence selected from the group consisting of sequences shown in SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 64 and SEQ ID NO: 65.

12. (Amended) An adenovirus vector packaging cell line, comprising:

Ep i) a stably integrated nucleic acid molecule, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleic sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon; and

ii) an operatively-linked promoter and a nucleic acid sequence that encodes an adenovirus structural protein,

wherein the sequence of nucleotides that encodes the TPL consists essentially of a first TPL exon operatively linked to a complete second TPL exon operatively linked to a complete third TPL exon.

21. (Amended) The cell line of claim 12, wherein said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome.

E7 22. (Once Amended) The cell line of claim 21, wherein said cell line expresses an adenovirus early protein gene and a fiber gene.

23. (Amended) The cell line of claim 21, wherein deletion of a deficient viral gene is complemented by the expression of a gene under the control of an inducible promoter.

47. (Amended) The method of claim 41, wherein:

E3 said nucleic acid molecule is a nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide

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sequence comprising (a) first and second different TPL exons or (b) first, second and third different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3; and

said molecule further comprises a sequence encoding adenovirus fiber protein.

96. (Amended) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises:

a) a stably integrated nucleic acid molecule, comprising:

a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises: (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, wherein said TPL exons are selected from the group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3; and

b) said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome; and

2) producing said adenovirus particle.

97. (Amended) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises: the stably integrated nucleic acid molecule, comprising:

a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides